Chapter 2.4.5 – Maedi-Visna

General comment for consideration: Each of the currently known small ruminant lentiviruses were named based on their clinical expression. However, molecular genetics is showing that, at the genome level, these viruses are notso easily distinguishable from each other, and may in fact be "quasi-species" of the same virus. Nevertheless, until we have an understanding of why sheep present with different clinical pictures (Maedi visna vs Ovine Progressive Pneumonia), we should maintain the naming based on clinical presentation, particularly for international trade purposes. We should note that given our current inability to distinguish the small ruminant lentiviruses by serological means, we should, therefore, consider them as "quasi-species" for eradication purposes.

Current text as proposed in the July 2003 Report:

Article 2.4.5.2.bis

Country or zone free from maedi-visna

A country or zone may be considered free from maedi-visna (MV) if:

1) it has a record of regular and prompt disease reporting in all livestock;

2) it has reported no clinical, epidemiological, serological or other evidence of MV during the past 5 years;

3) MV is notifiable in the whole country, and all clinical *cases* suggestive of MV are subjected to field and laboratory investigations;

4) all imports of sheep (except for slaughter) from other countries or zones over the past 5 years originated from an MV free country, zone or flock;

5) all sheep semen and embryos/ova imported for the past 5 years met the requirements referred to in Article 2.4.5.6 and in Article 2.4.5.7, respectively.

Suggested text:

Article 2.4.5.2.bis

Country or zone free from maedi-visna

A country or zone may be considered free from maedi-visna (MV) if:

1) it has a record of regular and prompt disease reporting in all livestock;

2) it has reported no clinical, epidemiological, serological or other evidence of MV during the past 5 years;

3) MV is notifiable in the whole country, and all clinical *cases* suggestive of MV are subjected to field and laboratory investigations;

4) all imports of sheep (except for slaughter) from other countries or zones over the past 5 years originated from an MV free country, zone or flock;

5) all sheep ~~semen~~ and embryos/ova imported for the past 5 years met the requirements referred to in Article 2.4.5.6 and in Article 2.4.5.7, respectively.

Rationale: there is no clear published evidence indicating that Maedi-Visna is transmitted by semen.

Current text as proposed in the July 2003 Report:

Article 2.4.5.6.

Veterinary Administrations of *importing countries* should require:

for ovine semen

the presentation of an *international veterinary certificate* attesting that:

1) the donor animals were resident for a minimum period of 5 years immediately prior to the time of semen collection in an MV free country, zone or flock;

2) the semen was collected, processed and stored in conformity with the provisions of Appendix 3.2.2.

Suggested text:

~~Article 2.4.5.6.~~

~~*Veterinary Administrations* of *importing countries* should require:~~

~~for ovine semen~~

~~the presentation of an *international veterinary certificate* attesting that:~~

~~1) the donor animals were resident for a minimum period of 5 years immediately prior to the time of semen collection in an MV free country, zone or flock;~~

~~2) the semen was collected, processed and stored in conformity with the provisions of Appendix 3.2.2.~~

Rationale: there is no clear published evidence indicating that Maedi-Visna is transmitted by semen.

The following comments address text contained in the "Supporting Document on Maedi-visna:

SUPPORTING DOCUMENT ON MAEDI-VISNA

1. Introduction

Ovine lentiviruses, maedi-visna virus (MVV) and South African ovine maedi-visna virus (SA-MVV), can infect sheep causing maedi-visna disease (MV) (Banks *et al*, 1983). The ovine lentiviruses are closely related to, but genetically and serologically distinct from, caprine arthritis encephalitis virus (CAEV) (Pasick, 1998; Valas *et al*, 2000).

Comment: Suggest starting the introduction with small ruminant lentiviruses including caprine arthrits-encephalitis virus (CAEV), maedi-visna virus (MVV), and ovine progressive pneumonia virus (the North American equivalent to MVV). Eradication of MVV or OPPV will only be successful if it also includes eradicating CAEV. Inappropriate use of reference Banks et al., 1983 for the sentence stated.

Comment: The ovine lentiviruses are related genetically to CAEV, but in some serological diagnostic tests, are not serologically distinct from CAEV (see Herrmann et al., 2003 in Clin.Diagnostic Laboratory Immunol.(CDLI) v.10, 267-271 and Herrmann et al., 2003 in CDLI v. 10, 862-865). Restate this sentence to make it less misleading.

2. Current world situation

It is difficult to assess the prevalence of MV globally because in some countries the disease is not reported. This may be due to the nature of the disease, which is usually latent and expressed mainly in older animals. Some under-reporting of MV may be due to alternative names for the disease; ovine progressive pneumonia, Montana sheep disease, zwoegersiekte, la bouhite, lungers, Marsh's progressive pneumonia and Graaff-Reinet disease.

3. Clinical signs

MV is a slowly progressive, insidious disease of sheep usually manifested either in the respiratory or central nervous system (CNS). Experimental infection can result in acute disease in young animals with very high mortality (Andresson *et al*, 1993).

Differential diagnosis

The disease must be differentiated from other causes of chronic respiratory and nervous system disease, including pulmonary adenomatosis, parasitic pneumonia, chronic bacterial pneumonia, scrapie, listeriosis, pregnancy toxaemia, plant poisoning and parasitic CNS invasion, e.g. *Coenuris cerebralis*.

4. Pathology

Lymphoproliferation caused by MVV may affect the lungs, mediastinal lymph nodes, brain, joints and mammary glands (Verwoerd *et al*, 1994). Demyelination in the presence of leucoencephalomyelitis is common in the central nervous system. The lymphocytic component of the inflammatory infiltrates is thought to be responsible for the observed neurological damage (Sanders *et al*, 2001). Not all strains of MVV lead to progressive encephalopathy (Campbell and Robinson, 1998).

5. Epidemiology

Spread

Sihvonen *et al* (1999) warns that if introduced into a free country, MV can spread widely before clinical cases are detected. This has happened in Iceland, Sweden and

Finland (Fridriksdottir *et al*, 2000; Hugoson, 1978; Sihvonen *et al*, 2000). In Sweden the disease was first recognised in 1974 and by 1975, a limited survey revealed 23 flocks were positive (Hugoson, 1978). The introduction of MV into Finland was traced to the importation of infected seronegative sheep in 1981 (Sihvonen *et al*, 1999).

Course of infection

MVV infections are characterised by a long and variable incubation period and life-long viral persistence (Cutlip *et al*, 1988) and clinical signs are rarely seen in sheep less than 3 years old

(Constable *et al*, 1996). The antibody response confers no resistance to disease and the clinical course of disease is progressive (Carey and Dalziel, 1993; Verwoerd *et al*, 1994).

Viraemia develops shortly after infection and plays a major role in distribution of monocyte associated virus throughout the body (Georgsson, 1990).

Prevalence

Studies in Canada, the United States of America (USA) and some countries of the European Union have shown the average flock seroprevalence of MV can range from 19% to 97% (Constable *et al*, 1996; Lujan *et al*, 1993; Houwers *et al*, 1987).

Comment: Include Cutlip et al., 1992 Am. J. Vet Res. v53, 976-979.

Lateral transmission

The target cells for MVV replication are mononuclear cells and transmission of virus occurs via these cells (Joag *et al*, 1996). Transmission predominantly occurs from ewe to lamb via ingestion of colostrum (Sihvonen, 1980). Lateral transmission can also occur during close contact, mainly via respiratory secretions. This form of spread is enhanced if an animal is coinfected with other pulmonary infections, particularly pulmonary adenomatosis.

Comment: Suggested sentence : One study has indicated that transmission occurs from ewe to lamb via ingestion of colostrum Sihvonen, 1980).

Vertical transmission – via embryos

The evidence for transplacental transmission of MVV is equivocal. Preventing colostral transfer and early contact with infected dams has been regarded as an effective means of obtaining MV free progeny (De Boer *et al*, 1979; Cutlip *et al*, 1988; Sihvonen, 1980). Long-term absence of MVV infection was demonstrated in a group of approximately 40 lambs separated from infected ewes immediately after birth and reared in isolation (De Boer *et al*, 1979). Similar results were reported by Light *et al* (1979) and Houwers *et al* (1987). Other studies suggest that the potential for transplacental infection cannot be entirely dismissed. Cutlip *et al* (1981) reported prenatal transmission based on the detection of MVV from 1 foetus and 2 newborn lambs out of 70 progeny. Cross *et al* (1975) reported infection in a small proportion of hysterectomy derived lambs from infected dams. More recently, Brodie *et al* (1994) detected MVV DNA in the peripheral blood mononuclear cells (PBMC) of 11% of lambs removed from their infected dams immediately after birth.

Viraemia which develops shortly after infection might expose embryos to virus. Using PCR techniques, Woodall *et al* (1993) failed to detect MVV in either uterine washes or washed embryos collected from 10 infected ewes. Further studies, involving increased numbers of animals at different stages of infection, are required to conclude that exposure of embryos to MVV during infection does not occur.

Vertical transmission – via semen

Transmission of infection via semen has not been demonstrated (Dawson, 1987). However, ovine lentivirus was detected in the semen of rams concurrently infected with *Brucella ovis* (de la Concha-Bermejillo *et al*, 1996). These authors suggest that inflammatory lesions of the genital tract causing leucocytospermia, as caused by *B. ovis*, predispose infected rams to shed ovine lentivirus in their semen. Moreover, semen may contain blood or plasma and MVV capsid antigen has been detected in plasma of infected sheep (Brodie *et al*, 1994). These studies do not provide clear evidence that MVV is transmitted to recipient ewes or offspring via infected semen but do suggest the potential for venereal transmission.

Breed susceptibility

Differences in breed susceptibility to MVV have been reported (Houwers *et al*, 1989). Icelandic breeds appear to be more susceptible than British breeds and Texels and Border Leicester are more susceptible to disease than Columbia sheep (Cutlip *et al*, 1986; Joag *et al*, 1996). Also, Snowder *et al* (1990) determined significant differences in the seroprevalence of MV between the 6 breed types comprising a flock of 2,976 sheep. Nevertheless, complete breed-associated resistance has not been demonstrated (Houwers, 1990). Houwers *et al* (1989) suggest that apparent susceptibility may also depend on the strain of MVV.

Host range

Disease due to MVV has only been reported in sheep and very rarely in goats (Castro *et al*, 1999; Banks *et al*, 1983).

Comment: Some recent evidence shows that some lentiviruses isolated from sheep genetically look more like CAEV (Karr et al., 1996, Virology v.225, 1-10 and Leroux et al., 1997, Arch Virol. V.142, 1125-1137); and, that some lentiviruses isolated from goats genetically look more like MVV (Roland et al., 2002, Virus Research v.85, 29-39). This strongly indicates that eradication will only be sucessful if all SRLVs (CAEV, MVV, and OPPV) are monitored.

6. Adverse consequences of MVV

A significantly lower reproduction rate was observed in seropositive ewes and their lambs suffered from significantly higher death and lower growth rates, probably due to a reduced milk production, resulting in economic losses (Scheer-Czechowski *et al*, 2000). This observation contrasts with that of Dungu *et al* (2000) who reported minimal difference between the pre-weaning growth of lambs born of ewes naturally infected with South African strains of maedi visna virus (MVV) and uninfected ewes kept under similar conditions.

In general, introduction of the MVV into a free country or zone results in an adverse economic impact. In most situations, the disease causes significant losses due to deaths, 'ill thrift' and the cost of control and eradication measures. In recognition of this adverse impact, eradication programmes have been implemented in the

Netherlands (Houwers, 1990), Canada (Williams-Fulton and Simard, 1989), Iceland (Zanoni *et al*, 1994), Finland (Sihvonen *et al*, 1999), Sweden (Lindqvist, 1994), USA (Young, 1993) and Germany (Scheer-Czechowski *et al*, 2000).

7. Risk management

a) Disease freedom of animals in country, zone or flock

Country/zone freedom

Reporting country status to the OIE with respect to MV is currently unreliable (Brodie *et al*, 1994; Constable *et al*, 1996; Handistatus II). Reliance on country or zone freedom as an effective risk management option therefore requires the specification of extra measures to ensure that a country or zone claiming freedom has adopted strategies to ensure this to be the case. MV should be notifiable in the whole country, and all clinical cases suggestive of MV should be thoroughly investigated. If serosurveys are not conducted, measures to prevent the introduction of the disease via animals or their genetic products should have been in place for at least 5 years. This period of time is expected to allow expression of disease if present in flocks before controls were implemented.

Flock freedom

Because serological testing is not always reliable and the disease has a long latency period, assurances of flock freedom within an infected country or zone may be difficult. Johnson *et al* (1992) observed that the absence of clinical signs over a 5year period alone can not be regarded as evidence of flock freedom. Similarly, Williams-Fulton and Simard (1989)advise that a longer time period than 4 years is required to ensure that MV has been completely eradicated from a flock. Houwers (1990) recommends certification of MVV freedom for flocks based on recent serological examination of the whole flock with negative results. Continuous surveillance was found to be necessary during the eradication programme in the Netherlands. This was expected due to the delay or absence of seroconversion in some infected animals (Houwers *et al*, 1987).

Sihvonen *et al* (1999) advise that surveillance of MV has to be continuous, requiring extensive, repeated serological testing and restrictions on the movement of sheep between flocks.

b) Embryo washing

Limited studies indicate that MVV does not transmit from infected sheep through transfer of embryo (Dawson and Wilmot, 1988; Young, 1993). IETS (1998) regard this disease agent as Category 4 in sheep (that is, “Diseases or disease agents on which preliminary work has been conducted or is in progress”).

c) **Testing and examination**

Clinically normal infected animals may be detected by serology or virus isolation, however both techniques can be unreliable.

Period from infections to antibody development

The period between exposure to virus and the detection of antibodies varies with the route of infection, form of exposure and breed of sheep. Seroconversion occurs from 4 to 6 weeks following experimental infection and antibody levels tend to stay relatively constant (Petursson, 1990). The first appearance of antibodies following natural infection can range from 11 months to over 5 years (Houwers *et al*, 1987). Persistent high antibody titres are usual in infected animals but disease in the absence of positive serology has been described (Houwers *et al*, 1987). A complicating factor is that significant viral antigenic variation can occur in MVV infected animal over time (Narayan *et al*, 1977). Also, the serological response to MVV varies with age and breed of sheep (Constable *et al*, 1996).

Sihvonen *et al* (1999) documents the failure of quarantine measures to prevent introduction of the disease into Finland. Introduction of infected seronegative sheep in 1981 were thought to be responsible for introduction of the disease, detected 13 years later during serosurveillance (Sihvonen *et al*, 1999).

Age effects

Viral RNA can be detected in PBM cells taken from naturally infected lambs less than 1 year of age by *in situ* hybridisation. However, animals less than 1 year of age rarely show seropositivity when infected (Johnson *et al*, 1992) and an increased seroprevalence occurs with age (Simard and Morley, 1991). Snowder *et al* (1990) determined the average seroprevalence to be 11% at one year of age and 93% in sheep 7 years or older. Cutlip *et al* (1992) found that prevalence increased from 4% at less than 1year to 34 % at 4 years, with variability associated with breed type.

Available serological tests

The agar gel immunodiffusion (AGID) test and the enzyme linked immunosorbent assay (ELISA) are the most commonly used serological tests (Simard and Briscoe, 1990). The sensitivity of both tests is dependent on the antigen used (Knowles, 1997; Rosati *et al*, 1994; Saman *et al*, 1999).

Comment: A new caprine-arthritis encephalitis virus (CAEV) competitive inhibition enzyme-linked immunosorbent assay (cELISA) has shown high sensitivity and specificity in both CAEV-infected goat herds and OPPV-infected sheep flocks using immunoprecipitation of ^{35}[S]methionine-labeled viral lysates as the standard of comparison (Herrmann et al., 2003, Clinical and Diagnostic Laboratory Immunology (CDLI), v. 10, 267-271 and Herrmann et al., 2003 CDLI, v. 10, 862-865).

Other detection methods

MV virus can be detected by virus isolation or nucleic acid detection methods. Even though virus cannot be recovered directly from tissue homogenates virus can be detected if explanted or by co-cultivating with a permissive cell type (Carey and Dalziel, 1993). A number of polymerase chain reaction (PCR) assays have been described which detect MV DNA in infected tissues, especially bone marrow, PBM cells and pulmonary leucocytes (Brodie *et al*, 1992;

Celer *et al*, 2000; Johnson *et al*, 1992). A PCR test has been used to detect infected sheep in the Dutch National MVV/CAEV control programme (Wagter *et al*, 1998).

Summary – the reliability of serological testing for detecting infected animals

Viral infections are characterized by a window period during which the host is infected but diagnostic test (e.g. antibody) results are negative. Animals determined to be infected by *in situ* hybridisation, PCR and co-cultivation were negative on serology (Johnson *et al*, 1992). Infection of other animals can occur during this period of seronegativity. To detect infections reliably, it is important to conduct antibody tests after the host animal has been given sufficient time to mount a detectable immune response. Houwers *et al* (1987) based accreditation of flocks on testing for MVV antibodies twice with an interval of 6months. However, eradication efforts in Finland relied on five consecutive serological tests at 12 to 16 month intervals. Repeated testing of all animals over 1 year of age was determined to be necessary because of the lack of sensitivity of serological testing. It was reasoned that if infected animals were missed, transmission would occur and eventually produce seropositive animals within the flock (Sihvonen *et al*, 2000).

In summary, the time required for seroconversion following infection can be relatively prolonged and unpredictable. An infected animal may give a negative result to a single antibody test so more than one test over a period, and reliance on flock testing rather than individual animal testing would be expected to increase the likelihood of sourcing non-infected animals.

REFERENCES

ANDRESSON O.S., ELSER J.E., TOBIN G.J., GREENWOOD J.D., GONDA M.A., GEORGSSON G., ANDRESDOTTIR V., BENEDIKTSDOTTIR E., CARLSDOTTIR H.M. and MANTYLA E.O. (1993) - Nucleotide sequence and biological properties of a pathogenic proviral molecular clone of neurovirulent visna virus. *Virology*, **193,** 89-105.

BANKS K.L., ADAMS D.S., MCGUIRE T.C. and CARLSON J. (1983) - Experimental infection of sheep by caprine-arthritis encephalitis virus and goats by progressive ovine pneumonia virus. *Am. J. Vet. Res*., **44**, 2307-2311.

BRODIE S.J., PEARSON L.D., SNOWDER G.D. and DEMARTINI J.C. (1993) - Host-virus interaction as defined by amplification of viral DNA and serology in lentivirus-infected sheep. *Arch. Virol.*, **130**, 413-428.

BRODIE S.J., DE LA CONCHA-BERMEJILLO A., KOENIG G., SNOWDER G.D. and DEMARTINI J.C. (1994) - Maternal factors associated with prenatal transmission of ovine lentivirus. *J. Infect. Dis.*, **169**, 653-657.

CAMPBELL R.S.F. and ROBINSON W.F. (1998) - The comparative pathology of the lentiviruses. *J. Comp. Path*., **119**, 333-395.

CAREY N. and DALZIEL R.G. (1993) - The biology of maedi-visna- an overview. *Br. Vet. J.*, **149**, 437-453.

CASTRO R.S., GREENLAND T., LEITE R.C., GOUVEIA A., MORNEX J.F. and CORDIER G. (1999) - Conserved sequence motifs involving the tat reading frame of Brazilian caprine lentiviruses indicate affiliations to both caprine arthritis-encephalitis virus and visna-maedi virus. *J. Gen. Virol.*, **80**, 1583-1589.

CELER V.JR., CELER V., NEJEDLA E., BERTONI G., PETERHANS E. and ZANONI R.G (2000) - The detection of proviral DNA by semi-nested polymerase chain reaction and phylogenetic analysis of Czech Maedi-Visna isolates based on gag gene sequences. *J. Vet. Med. B Infect. Dis. Vet. Public Health*, **47**, 203-215.

CONSTABLE P.D., MEIER W.A., FOLEY G.L., MORIN D., CUTLIP R.C. and ZACHARY J.F. (1996) - Visna-like disease in a ram with chronic demyelinating encephalomyelitis. *JAVMA*, **208**, 117-120.

CROSS R.F., SMITH C.K. and MOORHEAD P.D. (1975) - Vertical transmission of progressive pneumonia (maedi) in sheep. *Am. J. Vet. Res.*, **36**, 465-468.

CUTLIP R.C., LEHMKUHL H.D. and JACKSON T.A. (1981) - Intrauterine transmission of ovine progressive pneumonia virus. *Am. J. Vet. Res.*, **42**, 1795-1797.

CUTLIP R.C., LEHMKUHL H.D., BROGDEN K.A. and SACKS J.M. (1986) - Breed susceptibility to ovine progressive pneumonia (maedi/visna) virus. *Vet. Microbiol.*, **12**, 283-288.

CUTLIP R.C., LEHMKUHL H.D., SCHMERR M.J. and BROGDEN K.A. (1988) - Ovine progressive pneumonia (maedi-visna) in sheep. *Vet. Microbiol.*, **17**, 237-250.

CUTLIP R.C. (1992) - Seroprevalence of ovine progressive pneumonia virus in sheep in the United States as assessed by analyses of voluntarily submitted samples. *Am. J. Vet. Res.*, **53**, 976-979.

DAWSON M. (1987) - Pathogenesis of maedi-visna. *Vet. Rec.*, **120**, 451-454.

DAWSON M. and WILMOT P.L. (1988) - quoted in Parsonson I (1989) Scientific review of Australian quarantine protocols for importation of sheep and goat embryos. Working paper No.5/89, Bureau of Rural Resources, Canberra.

DE BOER G.F., TERPESTRA C., HENDRINKS J. and HOUWERS D.J. (1979) - Studies in epidemiology of maedi-visna in sheep. *Res. Vet. Sc.*, **26**, 202-208.

DE LA CONCHA-BERMEJILLO A., MAGNUS-CORRAL S., BRODIE S.J. and DEMARTINI J.C. (1996) - Venereal shedding of ovine lentivirus in infected rams. *AVJR*, **57**, 684-688.

DUNGU B., VORSTER J., BATH G.F. and VERWOERD D.W. (2000) - The effect of a natural maedi-visna virus infection on the productivity of South African sheep. *Onderstepoort J. Vet. Res.*, June **67** (2), 87-96.

FRIDRIKSDOTTIR V., GUNNARSSON E., SIGURDARSON S. and GUDMUNDSDOTTIR K.B. (2000) - Paratuberculosis in Iceland: epidemiology and control measures, past and present. *Vet. Microbiol.*, **77**, (3-4), 263-267.

GEORGSSON G. (1990) - Maedi-visna pathology and pathogenesis. *In*: Maedi-visna and related diseases. Petursson G. and Hoff-Jorgensen R., eds Kluwer Academic Publishers, 19-54.

HOUWERS D.J. (1990) - Economic importance, epidemiology and control. *In*: Maedi-Visna and related diseases. Petursson G. and Hoff-Jorgensen R., eds Kluwer Academic Publishers, 83-117.

HOUWERS D.J. and VAN DER MOLEN E.J. (1987) - A five-year serological study of natural transmission of maedi-visna virus in a flock of sheep, completed with post mortem examination. *J. Vet. Med. B*, **34**, 421-431.

HOUWERS D.J., KONIG C.D., BAKKER J., DE BOER M.J., PEKELDER J.J., SOL J., VELLEMA P. and DE VRIES G. (1987) - Maedi-visna control in sheep. III: Results and evaluation of a voluntary control program in the Netherlands over a period of four years. *Vet. Q.*, Nov. 9, Suppl 1, 29S-36S.

HOUWERS D.J., VISSCHER A.H. and DEFIZE P.R. (1989) - Importance of ewe/lamb relationship and breed in the epidemiology of maedi-visna virus infections. *Res. Vet. Science*, **46**, 5-8.

HUGOSON G. (1978) - Maedi in Sweden. *Bulletin* de l'Office International des Epizooties, 1978, 89: 7-8, 445-449.

JOAG S.V., STEPHENS E.B. and NARAYAN O. (1996) - Lentiviruses. *In*: Fields virology, third edition, Fields B.N., Kapie D.M., Howley P.M. *et al.*, eds. Lippincott- Raven Publishers, Philadelphia, 1977-1999.

JOHNSON L.K., MEYER A.L. and ZINK M.C. (1992) - Detection of ovine lentivirus in seronegative sheep by in situ hybridization, PCR and cocultivation with susceptible cells. *Clin. Immunol. Immunopathol.*, **65**, 254-260.

KNOWLES D.P. JR. (1997) - Laboratory diagnostic tests for retrovirus infections of small ruminants. *Vet. Clin. North Am. Food Anim. Pract.*, **13**, 1-11.

LIGHT M.R., SCHIPPER I.A., MOLITOR T.W., TILTON J.E. and SLANGER W.D. (1979) - Progressive pneumonia in sheep: incidence of natural infection and establishment of clean flocks. *J. Anim. Sc.*, **49**, 1157-1160.

LINDQVIST A. (1994) - Very good support for the visna maedi control programme. *Svensk-Veterinartidning*, **10**, 437-439.

LUJAN L., BADIOLA J.J., GARCIA-MARIN J.F., MORENO B., VARGAS M.A., FERNANDEZ DE LUCO D. and PEREZ V. (1993) - Seroprevalence of maedi-visna infection in sheep in the north-east of Spain. *Preventive Veterinary Medicine*, **15**, 181-190.

NARAYAN O., GRIFFIN D.E. and CHASE J. (1977) - Antigenic shift of visna virus in a persistently infected sheep. *Science*, **197**, 376-378.

PASICK J. (1998) - Use of a recombinant maedi-visna virus protein ELISA for the serologic diagnosis of lentivirus infections in small ruminants. *Can. J. Vet. Res.*, **62**, 307-310.

PETURSSON G. (1990) - Maedi-visna. Etiology and immune response. *In*: Maedi-visna and related diseases, Petursson G. and Hoff-Jorgensen R., eds Kluwer Academic Publishers, 55-71.

ROSATI S., KWANG J., TOLARI F. and KEEN J. (1994) - A comparison of whole virus and recombinant transmembrane ELISA and immunodiffusion for detection of ovine lentivirus antibodies in Italian sheep flocks. *Veterinary Research Communications*, **18**, 73-80.

SAMAN E., VAN EYNDE G., LUJAN L., EXTRAMIANA B., HARKISS G., TOLARI F., GONZALEZ L., AMORENA B., WATT N. and BADIOLA (1999) - A new sensitive serological assay for detection of lentivirus infections in small ruminants. *J. Clin. Diagn. Lab. Immunol.*, **6**, 734-740.

SANDERS V.J., WILEY C.A. and HAMILTON R.L. (2001) - The mechanisms of neuronal damage in retroviral infections of the nervous system. *Current Topics in Microbiology and Immunology*, **253**, 179-201.

SCHEER-CZECHOWSKI P., VOGT H.R., TONTIS A., PETERHANS E. and ZANONI R. - Schweiz Arch Tierheilkd 2000 Apr, **142** (4), 155-164 [Pilot project for eradicating maedi-visna in Walliser blacknose sheep].[Article in German]

SIHVONEN L., HIRVELA-KOSKI V., NUOTIO L. and KOKKONEN U.M. (1999) - Serological survey and epidemiological investigation of maedi-visna in sheep in Finland. *Vet. Microbiol.*, **65**, 265-270.

SIHVONEN L., NUOTIO L., RIKULA U., HIRVELA-KOSKI V. and KOKKONEN U.M. (2000) - Preventing the spread of maedi-visna in sheep through a voluntary control programme in Finland. *Prev. Vet. Med.*, **47**, 213-220.

SIHVONEN L. (1980) - Studies on transmission of maedi virus to lambs. *Acta Vet. Scandinavica*, **21**, 689-698.

SIMARD C. and MORLEY R.S. (1991) - Seroprevalence of maedi-visna in Canadian sheep. *Can. J. Vet. Res.*, Jul **55** (3), 269-273.

SIMARD C.L. and BRISCOE M.R. (1990) - An enzyme-linked immunosorbent assay for detection of antibodies to maedi-visna virus in sheep. A simple technique for production of antigen using sodium dodecyl sulfate treatment. *Can. J. Vet. Res.*, **54**, 446-450.

SNOWDER G.D., GATES N.L., GLIMP H.A. and GORHAM J.R. (1990) - Prevalence and effect of subclinical ovine progressive pneumonia virus infection on ewe wool and lamb production. *J. Am. Vet. Med. Assoc.*, **197**, 475-479.

VALAS S., BENOIT C., BAUDRY C., PERRIN G. and MAMOUN R.Z. (2000) - Variability and immunogenicity of caprine arthritis-encephalitis virus surface glycoprotein. *J. Virol.*, **74**, 6178-6185.

VERWOERD D.W., TUSTIN R.C. and WILLIAMSON A.L. (1994) - Maedi-visna. *In*: Infectious Diseases of Livestock with special reference to Southern Africa. Coetzer J.A.W., Thomson G.R. and Tustin R.C., eds. Oxford University Press, Southern Africa, Capetown, Vol. 2, 792-796.

WAGTER L.H., JANSEN A., BLEUMINK-PLUYM N.M., LENSTRA J.A. and HOUWERS D.J. (1998) - PCR detection of lentiviral GAG segment DNA in the white blood cells of sheep and goats. *Vet. Commun*., **22**, 355-362.

WILLIAMS–FULTON N.R. and SIMARD C.L. (1989) - Evaluation of two management procedures for the control of maedi-visna. *Can. J. Vet. Res*., **53**, 419-423.

WOODALL C.J., MYLNE M.J.A., MCKELVEY W.A.C. and WATT N.J. (1993) - Polymerase chain reaction (PCR) as a novel method for investigating the transmission of maedi-visna virus (MVV) by pre-implantation embryos. *In*: Proc. 3rd International Sheep Veterinary Congress, Edinburgh, June 1993, 232.

YOUNG S. (1993) - Progress towards eradication of ovine progressive pneumonia from the Iowa State University teaching flocks. *In*: Proc. 11th Annual Meeting of Iowa Veterinary Medical Association, 22-24 January 1993.

ZANONI R.G., VOGT H.R., POHL B., BOTTCHER J., BOMMELI W. and PETERHANS E. (1994) - An ELISA based on whole virus for the detection of antibodies to small-ruminant lentiviruses. *Zentralbl Veterinarmed* [B], **41**, 662-669.

ZANONI R.G. (1998) - Phylogenetic analysis of small ruminant lentiviruses. *J. Gen. Virol*.,**79**,1951-1961.